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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,402	10/16/2003	Jaya Sivaswami Tyagi	AP35478 066123.0125	8618

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BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,402	TYAGI ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *8-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-9-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are pending.

Election/Restrictions

Applicant's election with traverse of Group I invention, claims 1-7, and the species wherein $DevS_{578}$ is the DevS derivative, $Rv2027_{194}$ is the Rv2027 derivative, and $DevRN_{145}$ is the DevR derivative, in the reply filed December 9, 2004, is acknowledged. The traversal is on the grounds that for Groups I-III the field of search would not differ one from the other and that there is a single, searchable unifying relationship. This is not found persuasive because, as pointed out in the restriction requirement, the methods claimed in Groups I and II and the compositions claimed in Group III are not required one for the other even though they both involve DevR-DevS and/or DevR-Rv2027c or homologues thereof. The methods of Groups I and II require different materials and different steps, thus necessitating separate fields of search. Specifically, drugs used to accomplish the methods of Group II are not required to go through the screening steps of Group I.

As stated in the restriction, the compositions of Group III are not required for Group I, as the compositions of Group III may not be discovered through applying the methods of Group I. Compositions treating disease conditions caused by pathogenic microbes with a particular signal transduction system may not act on the signal transduction system themselves. Finally, while Groups II and III are placed in the same class, the products of Group III may be used in materially different processes and, as noted above, may not act on DevR-DevS or DevR-Rv2027c.

As to the argued lack of "serious" burden, the present claims encompass compositions for controlling disease conditions, to a screening assay, to a method of treating disease conditions. Thus, any argument regarding lack of burden clearly ignores the very broad subject matter encompassed by the current claims and the significant burden on search and examination presented thereby.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. As noted immediately above, applicant timely traversed the restriction (election) requirement in the reply filed on December 9, 2004.

Claims 1-7 are examined on the merits to the extent they read on the elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identification of anti-tuberculosis and anti-mycobacterial compounds, does not reasonably provide enablement for identification of compounds that may be used to treat

disease conditions caused by bacteria such as pneumonia, pertussis, listeriosis, enterobacterial diseases, and cholera. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Regarding undue experimentation, *In re Wands*, 8 USPQ2d 1400, at 1404 (Fed. Cir. 1988) states:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman.* They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (Citations omitted).

Claim 7 is drawn to a screening method for identifying a compound that inhibits growth of pathogenic microbes having DevR-DevS and/or DevR-Rv2027c and its homologues, wherein autophosphorylation and dephosphorylation are observed to assess test compounds. The specification discloses the presence of the DevR-DevS two-component system in *Mycobacterium tuberculosis*, *Mycobacterium bovis* BCG, and *Mycobacterium smegmatis* (page 6, lines 2-3). However, no indication is provided that DevR-DevS and/or DevR-Rv2027c and its homologues are present in other bacteria, nor is it known in the prior art.

The amount of direction provided in the specification does not speak on the procedures required to test various species of bacteria for the existence of DevR-DevS and/or DevR-Rv2027c and its homologues. Existence of these two-component systems is required for claim 7 since they are essential to the assessment of test compounds. In order to practice the claimed invention, a skilled artisan would have to determine the

presence of the indicated two-component systems in other bacteria causing diseases not limited to pneumonia, pertussis, listeriosis, enterobacterial diseases, and cholera. Given the lack of guidance from the specification and prior art, experimentation would be great since it would require testing a multitude of bacterial species and developing and proceeding through appropriate experimental methods for detecting the required two-component systems in each species.

Thus, a skilled artisan would have expected to have had to engage in an essentially trial and error process, with little guidance from the specification as filed. Such a trial and error process clearly constitutes undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 7, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The third line of claim 1 reads on a two-component system of the "homologues" of DevR-DevS and/or DevR-Rv2027c. The degree of similarity with DevR-DevS or DevR-Rv2027c encompassed in the term "homologues" is not clear, therefore the term fails to delineate the scope of two-component systems encompassed. In summary, the term is not defined by the

claim, the specification does not provide a standard for ascertaining the requisite degree of similarity, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus claims 1-7 are rejected under 35 U.S.C. 112, second paragraph.

Additionally, it is unclear how the overexpression of the signal transduction proteins in *E. coli* in claim 5 logically follows from the steps in claim 1. Thus claim 5 is rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoch et al. (US Patent 6,043,045) in view of Dasgupta et al. (2000, Tubercle and Lung Disease, 80(3): 141-159).

Hoch et al. discloses a method for identifying new antibiotic, antibacterial, or antimicrobial agents by inhibition of bacterial two-component systems. Specifically, agents are sought that cause the "inhibition of either the autophosphorylation or the subsequent phosphor-transfer" (column 2, lines 16-23). Furthermore, the conventional use of SDS-PAGE to assay two-component systems is described (column 2, lines 24-35). Hoch et al. provides a high-throughput screening assay for histidine protein kinase for agent identification (column 22, lines 16-24).

Hoch et al. does not expressly disclose the use of their methods for inhibition of DevR-DevS or DevR-Rv2027c and its homologues nor does it disclose the identification of anti-tuberculosis and anti-mycobacterial compounds.

Dasgupta et al. discloses the DevR-DevS two-component system in mycobacteria, specifically *M. tuberculosis*, as well as the homology of Rv2027c with DevS. It is obvious that $DevS_{578}$, $Rv2027_{194}$, and $DevRN_{145}$ would share common characteristics with DevS, Rv2027 and DevR respectively because, as evidenced by Dasgupta (Figure 3, page 148 and Figure 5, page 150), the claimed portions each contain the catalytic site of the molecules, based on the size of the transcripts disclosed in the reference.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to apply the methods of Hoch et al. to the DevR-DevS and the known homolog of

DevR-Rv2027c as described in Dasgupta et al. The DevR-DevS and DevR-Rv2027c systems both comprise a histidine protein kinase (DevS or Rv2027c), thus being appropriate as a target of the Hoch invention. By applying the Hoch invention to the DevR-DevS system, it would be obvious that an agent positively identified could be used for tuberculosis or other diseases caused by mycobacteria.

One of ordinary skill in the art would have been motivated to do this because Dasgupta et al. concludes that "the devR-devS two-component system may thus serve as a novel target for anti-tubercular therapy" (page 158, second paragraph). Tuberculosis is a critical issue, so there is a high incentive to develop or determine compounds for its treatment. There would have been a reasonable expectation of success that the Hoch invention could be used for bacteria such as *M. tuberculosis* that have DevR-DevS and/or DevR-Rv2027c and its homologues based on the fact that Hoch's assay techniques are disclosed as measuring the same reactions catalyzed by Dasgupta's tuberculosis phosphorylases. A holding of obviousness is therefore proper.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan E. Fernandez
Assistant Examiner
Art Unit 1651

sef

FRANCISCO PRATS
PRIMARY EXAMINER